

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
3 June 2004 (03.06.2004)

PCT

(10) International Publication Number
WO 2004/045688 A1

(51) International Patent Classification: **A61M 15/00**

[GB/GB]: GlaxoSmithKline, Park Road, Ware, Hertfordshire SG12 0DP (GB).

(21) International Application Number:
PCT/EP2003/013074

(74) Agent: **RICE, Jason, Neale**; GlaxoSmithKline, Corporate Intellectual Property (CN925.1), 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(22) International Filing Date:
18 November 2003 (18.11.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0227128.6 20 November 2002 (20.11.2002) GB

(71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NL, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

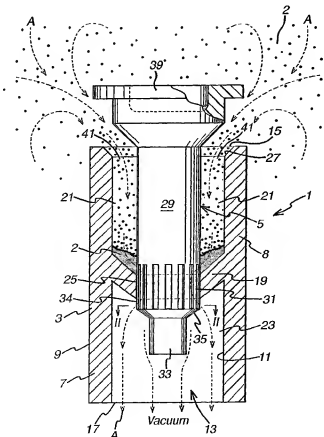
(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,

(72) Inventor; and

(75) Inventor/Applicant (for US only): **RAND, Paul, Kenneth**

[Continued on next page]

(54) Title: CAPSULE FOR A POWDER MEDICAMENT



(57) Abstract: A capsule (1) for a powder (2) has a body which is provided with an internal chamber (21) to hold the powder and first and second openings (17, 15) to an exterior environment. The body is adapted to be displaced from a filling state, in which the first and second openings are placed in fluid communication with one another through the internal chamber thereby enabling an airflow to be created through the body from the second opening (15) to the first opening which is able to entrain powder in the exterior environment into the internal chamber for filling thereof, to a sealing state in which the internal chamber is sealed from the exterior environment so as to retain the powder held therein.

WO 2004/045688 A1



SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

CAPSULE FOR A POWDER MEDICAMENT

Related Application

- 5 This application claims priority from UK patent application No. 0227128.6 filed 20 November 2002, the entire content of which is hereby incorporated herein by reference.

Field of the Invention

10

The present invention relates to a capsule for holding a powder and is particularly, but not exclusively, concerned with such a capsule for containing a pharmaceutical powder, for instance an inhalable pharmaceutical powder.

15 Background of the Invention

- Dry powder inhalation devices ("DPI" for short) are well established for use in treating respiratory diseases. As an example, there may be mentioned the DISKUS® device of GlaxoSmithKline. In general, the pharmaceutical composition
20 is formulated as a respirable powder and the powder is divided into a plurality of unit doses, each dose contained in its own sealed enclosure, for example blisters on a dosing strip. In use of the inhaler, the enclosures are opened, one at a time, by an opening mechanism of the inhalation device and the powder dose entrained into a patient's respiratory tract by an airflow generated through the
25 device by the patient inhaling at a mouthpiece of the device.

- Some of the sealed enclosures used in DPIs are difficult to fill with a unit dose of the pharmaceutical powder. It is an aim of the invention to provide a capsule for holding a powder which facilitates its filling with the powder.
30

As background art there may be mentioned WO01/07107, WO02/096489, US-A-2587215, US-A-4446862 and GB-A-2323042.

Summary of the Invention

According to the present invention there is provided a capsule for a
5 powder having a body which is provided with an internal chamber to hold the
powder and first and second openings to an exterior environment, the body
adapted to be displaced from a filling state, in which the first and second
openings are placed in fluid communication with one another through the internal
chamber thereby enabling creation of an airflow through the body from the
10 second opening to the first opening which is able to entrain powder in the exterior
environment into the internal chamber for filling thereof, to a sealing state in
which the internal chamber is sealed from the exterior environment so as to
retain the powder held therein.

15 The invention also provides a method of providing a capsule filled with a
powder having the steps of providing a capsule according to the invention in its
filling state, creating an airflow through the body of the capsule in a direction from
the second opening to the first opening to cause powder from a powder source
disposed externally of the capsule to be entrained into the internal chamber of
20 the body, and moving the capsule to its sealing state.

The airflow through the capsule body may be created by applying a
vacuum at the first opening of the capsule body.

25 Preferred features of the invention are set forth in the subordinate claims
appended hereto, as well as in the non-limiting exemplary embodiment of the
invention hereinafter described with reference to the accompanying FIGURES of
drawings.

Brief Description of the Drawings

FIGURE 1 is a part sectional side view of a capsule for a powder product in accordance with the present invention in a filling position, the capsule comprising a sleeve part and a piston part slidably mountable in the sleeve part.

FIGURE 2 is a cross-sectional view of the piston part along line II-II in FIGURE 1 showing a circumferential array of longitudinal channels formed in a portion of the outer surface of the piston part.

FIGURE 3 is a part sectional side view of the capsule showing the piston part in a sealed position in the sleeve part with the powder product contained in a sealed chamber defined between the piston and sleeve parts.

FIGURE 4 is a part sectional side view of the capsule with the piston part in a discharge position relative to the sleeve part.

Detailed Description of the Exemplary Embodiment of the Invention

In the FIGURES of drawings there is shown a generally cylindrical capsule 1 adapted to be filled with a powder product 2. The capsule 1 has particular application for dry powder products, more particularly dry powder pharmaceutical formulations for inhalation by a patient. The capsule 1 may be used in a dry powder inhaler.

The capsule 1 has a two-part construction comprising a generally cylindrical outer sleeve part 3 and a generally cylindrical inner piston part 5. The capsule 1 is preferably made from air- and moisture-proof materials, especially if the powder 2 is hygroscopic, as is the case with many pharmaceutical powders. Where the capsule is for a pharmaceutical powder, the material is an inert pharmaceutically acceptable material.

The outer sleeve part 3 has an annular wall 8 having an outer circumferential surface 9 and an inner circumferential surface 11. The inner circumferential surface 11 bounds an axial bore 13 which passes through the sleeve part 3 from an upper open end 15 to a lower open end 17. The upper
5 open end 15 has a countersunk entrance 27.

The inner circumferential surface 11 is shaped to define a restriction 19 in the bore 13 to divide the bore 13 into an upper section 21 and a lower section 23. The restriction 19 in this embodiment takes the form of a step or shoulder which
10 extends radially into the bore 13 to define an intermediate bore section 25 of narrower inner diameter than that of the upper and lower sections 21, 23. The restriction 19 in the bore 13 is resiliently deformable such that, on application of a downward force thereon, it is able to be deflected downwardly towards the lower open end 17 and, on release of the downward force, it returns to its undeformed
15 position. This allows the piston part 5 to be held in place in the sleeve part 3 in different sliding positions, and for a dynamic seal to be formed between the sleeve and piston parts 3, 5.

The sleeve part 3 is preferably made from a plastics material, for instance
20 by a moulding process, such as injection moulding or micro-moulding.

The sleeve part 3 may have a length (height) in the range of about 5mm to about 15mm and an outer diameter in the range of about 3mm to about 8mm. In other words, the capsule 1 may be referred to as a "microcapsule". The bore 13
25 may have an inner diameter (in the upper and lower sections 21, 23) in the range of about 1mm to about 6mm. Such a capsule 1 is suited for holding a unit dose of a pharmaceutical powder in the range of about 2 μ g to about 30mg. The capsule 1 may contain a unit dose of pure active drug substance, or a blend of pure active drug substances, in the range of about 2 μ g to about 250 μ g (i.e. no
30 bulk filler), or a bulked out unit dose of a pharmaceutical powder up to about 30mg.

For a small unit dose of pharmaceutical powder, for instance in the range of about 2-250 μ g, it is preferable for the sleeve part 3 to have a length (height) in the range of about 5mm to about 6mm, an outer diameter in the range of about 3mm to about 5mm, and an inner diameter in the range of about 1mm to about 3mm, more preferably about 2mm.

Turning now to the piston part 5, as shown in FIGURES 2 and 3 this has a shank 29 of a general cylindrical cross section. The shank 29 has an upper section 31, a lower section 33 of smaller outer diameter than the upper section 31, and a flared section 35 connecting the upper and lower sections 31, 33. A series of longitudinal grooves or flutes 37 is circumferentially arranged about a lower end portion 34 of the upper shank section 31.

As shown most clearly in FIGURE 4, the upper section 31 of the shank 29 has an outer diameter d1 which is the same, or, more typically, greater than the 'normal' inner diameter d2 of the intermediate section 25 of the bore 13 in the sleeve part 3. Thus, the upper section 31 of the shank 29 fits in the intermediate section 25 with an interference fit, the resiliently deformable nature of the restriction 19 facilitating the formation of the interference fit, especially when the outer diameter d1 of the upper section 31 of the shank 29 is greater than the inner diameter d2 of the intermediate section 25 of the bore 13. In this particular embodiment, the inner diameter d2 of the intermediate bore section 25 is less than the outer diameter d1 of the upper shank section 31, as will be appreciated by a comparison of FIGURES 3 and 4.

At an upper end of the shank 29 there is provided a co-axially arranged piston head 39 of larger outer diameter than the shank 29.

The piston part 5 is also preferably made from a plastics material, for instance by a moulding process, such as injection moulding or micro-moulding.

In use, the piston part 5 is first slidably mounted in the sleeve part 3 in a filling position shown in FIGURE 1. In the filling position, the upper section 31 of the shank 29 of the piston part 5 is slidably received in the intermediate section 25 of the bore 13 so as to be held in frictional engagement therewith such that the longitudinal grooves 37 place the upper and lower bore sections 21,23 in fluid communication with one another. In this regard, it will be noted that the longitudinal grooves 37 have a longer longitudinal dimension than that of the intermediate section 25 of the bore 13. Placing the piston part 5 in the filling position spaces the piston head 39 above the upper open end 15 of the bore 13, as further shown in FIGURE 1. In this way, an inlet path 41 into the upper section 21 of the bore 13 is defined.

With the piston part 5 in its filling position, application of a vacuum to the lower open end 17 of the sleeve part 3 draws powder particles 2 from a particle cloud in the exterior environment around the capsule 1 into the upper bore section 21 through the inlet path 41 as a result of the vacuum pressure acting in the upper bore section 21 through the longitudinal grooves 37. This is shown diagrammatically in FIGURE 1 by the arrows A.

The longitudinal grooves 37 are sized such that the powder particles 2 are occluded therein. This does not prevent the vacuum from creating the negative pressure in the upper bore section 21 in the filling position, but prevents the powder 2 from seeping from the upper bore section 21 to the lower bore section 23. As an example, the grooves 37 may have a depth in the range of substantially 0.005-0.01 mm, preferably substantially 0.007 mm.

Once the upper bore section 21 has been filled with the required dose of powder 2, for example a unit dose of a pharmaceutical powder, the vacuum is removed and the piston part 5 slid downwardly in the sleeve part 3 to a sealed position shown in FIGURE 3. The sliding movement of the piston part 5 to the sealed position results in:-

- (i) The longitudinal grooves 37 moving out of the intermediate bore section 25 into the lower bore section 23 to bring the upper shank section 31 into sealing, frictional engagement with the intermediate section 25.
- 5 (ii) The piston head 39 being brought into sealing engagement with the countersunk entrance 27 of the bore 13.

This prevents or inhibits ingress of air or moisture into the upper bore section 21 and prevents egress of the powder 2 from the capsule 1. So, in the
10 sealed position the powder 2 drawn into the upper bore section 21 is sealably contained therein.

When the dose of powder 2 in the upper bore section 21 is required to be discharged, the piston part 5 is slid upwardly to a discharge position shown in
15 FIGURE 4. In the discharge position of the piston part 5, the piston head 39 is spaced upwardly of the upper open end 15 of the sleeve part 3 and the lower section 33 of the shank 29 is positioned in the intermediate bore section 25. In this way, an airflow path indicated by the arrows B is provided which enables the powder 2 in the upper bore section 21 to be discharged from the capsule 1 out of
20 the upper open end 15 of the sleeve part 3. The powder 2 may be discharged in this way by application of a positive air pressure to the bore 13 of the sleeve part 3 through the lower open end 17.

The resilience of the restriction 19 will be appreciated by comparing the
25 angle θ that the restriction 19 makes with the inner circumferential surface 11 in the sealed state shown in FIGURE 3 with the 'return' or 'normal' angle α it makes in the discharging state shown in FIGURE 4.

Appropriate medicaments for the inhalable pharmaceutical powder for use
30 in the present invention may be selected from, for example, analgesics, e.g., codeine, dihydromorphine, ergotamine, fentanyl or morphine; anginal preparations, e.g., diltiazem; antiallergics, e.g., cromoglycate (e.g. as the sodium

salt), ketotifen or nedocromil (e.g. as the sodium salt); anti-infectives e.g., cephalosporins, penicillins, streptomycin, sulphonamides, tetracyclines and pentamidine; antihistamines, e.g., methapyrilene; anti-inflammatory, e.g., beclomethasone (e.g. as the dipropionate ester), fluticasone (e.g. as the propionate ester), flunisolide, budesonide, rofleponide, mometasone e.g. as the furoate ester), ciclesonide, triamcinolone (e.g. as the acetonide) or 6α , 9α -difluoro-11 β -hydroxy-16 α -methyl-3-oxo-17 α -propionyloxy-androsta-1,4-diene-17 β -carbothioic acid S-(2-oxo-tetrahydro-furan-3-yl) ester; antitussives, e.g., noscaphine; bronchodilators, e.g., albuterol (e.g. as free base or sulphate), salmeterol (e.g. as xinafoate), ephedrine, adrenaline, fenoterol (e.g. as hydrobromide), formoterol (e.g. as fumarate), isoprenaline, metaproterenol, phenylephrine, phenylpropanolamine, pirbuterol (e.g. as acetate), reproterol (e.g. as hydrochloride), rimiterol, terbutaline (e.g. as sulphate), isoetharine, tulobuterol or 4-hydroxy-7-[2-[[[3-(2-phenylethoxy)propyl]sulfonyl]ethyl]amino]ethyl-2(3H)-benzothiazolone; adenosine 2a agonists, e.g. 2R,3R,4S,5R)-2-[6-Amino-2-(1S-hydroxymethyl-2-phenyl-ethylamino)-purin-9-yl]-5-(2-ethyl-2H-tetrazol-5-yl)-tetrahydro-furan-3,4-diol (e.g. as maleate); α_4 integrin inhibitors e.g. (2S)-3-[4-({[4-(aminocarbonyl)-1-piperidiny]carbonyl}oxy)phenyl]-2-[[[(2S)-4-methyl-2-[(2-methylphenoxy) acetyl]amino]pentanoyl]amino] propanoic acid (e.g. as free acid or potassium salt), diuretics, e.g., amiloride; anticholinergics, e.g., ipratropium (e.g. as bromide), tiotropium, atropine or oxitropium; hormones, e.g., cortisone, hydrocortisone or prednisolone; xanthines, e.g., aminophylline, choline theophyllinate, lysine theophyllinate or theophylline; therapeutic proteins and peptides, e.g., insulin or glucagon; vaccines, diagnostics, and gene therapies. It will be clear to a person skilled in the art that, where appropriate, the medicaments may be used in the form of salts, (e.g., as alkali metal or amine salts or as acid addition salts) or as esters (e.g., lower alkyl esters) or as solvates (e.g., hydrates) to optimise the activity and/or stability of the medicament.

Preferred medicaments are an anti-inflammatory agent (for example a corticosteroid or an NSAID), an anticholinergic agent, a β_2 -adrenoreceptor agonists, an anti-infective agent (e.g. an antibiotic or an antiviral) and an

antihistamine. The medicament may be the sole medicament in the capsule or in combination with another medicament. Preferred combinations are based on the preferred medicament list above.

- 5 Preferred as a component of a medicament combination in the capsule are albuterol, salmeterol, fluticasone propionate and beclomethasone dipropionate and salts or solvates thereof, e.g., the sulphate of albuterol and the xinafoate of salmeterol.
- 10 A particularly preferred medicament combination for use in the capsule of the invention is a bronchodilator in combination with an anti-inflammatory. The bronchodilator is suitably a beta-agonist, particularly a long-acting beta-agonist (LABA). Suitable bronchodilators include salbutamol (e.g., as the free base or the sulphate salt), salmeterol (e.g., as the xinafoate salt) and formoterol (eg as the fumarate salt). The anti-inflammatory is suitably an anti-inflammatory steroid.
- 15 Suitable anti-inflammatory compounds include a beclomethasone ester (e.g., the dipropionate), a fluticasone ester (e.g., the propionate) or budesonide or any salt or solvate thereof. One preferred combination is fluticasone propionate and salmeterol, or any salt or solvate thereof (particularly the xinafoate salt). A
- 20 further preferred combination is budesonide and formoterol or any salt or solvate thereof (e.g. formoterol as the fumarate salt).

- Generally, powdered medicament particles suitable for delivery to the bronchial or alveolar region of the lung have an aerodynamic diameter of less
- 25 than 10 micrometers, preferably less than 6 micrometers. Other sized particles may be used if delivery to other portions of the respiratory tract is desired, such as the nasal cavity, mouth or throat. The medicament may be delivered as a pure drug or together with excipients (carriers) which are suitable for inhalation. Suitable excipients include organic excipients such as polysaccharides (i.e.
- 30 starch, cellulose and the like), lactose, glucose, mannitol, amino acids, and maltodextrins, and inorganic excipients such as calcium carbonate or sodium chloride. Lactose is a preferred excipient. The excipient may be included with the

medicament via well-known methods, such as by admixing, co-precipitating and the like.

5 Particles of the powdered medicament and/or excipient may be produced by conventional techniques, for example by micronisation, milling or sieving. Additionally, medicament and/or excipient powders may be engineered with particular densities, size ranges, or characteristics. Particles may comprise active agents, surfactants, wall forming materials, or other components considered desirable by those of ordinary skill.

10

 It will be understood that the embodiment described hereinabove may be varied and modified in many different ways and adopt other guises within the scope of the appended claims. With this in mind, the use of reference numerals in the appended claims is for illustration only, and not meant to have a limiting effect on the scope of the claims. Finally, the use of prefixes such as
15 "substantially" and "generally" etc. to numeric values, geometries and other parameters in the specification is meant to include the exact numeric value, geometry and parameter.

CLAIMS

1. A capsule (1) for a powder (2) having a body which is provided with an internal chamber (21) to hold the powder and first and second openings (17, 15)
5 to an exterior environment, the body adapted to be displaced from a filling state, in which the first and second openings are placed in fluid communication with one another through the internal chamber thereby enabling creation of an airflow through the body from the second opening (15) to the first opening which is able to entrain powder in the exterior environment into the internal chamber for filling
10 thereof, to a sealing state in which the internal chamber is sealed from the exterior environment so as to retain the powder held therein.
2. The capsule of claim 1 in which the filling and sealing states are, respectively, expanded and contracted states of the body.
- 15 3. The capsule of claim 1 or 2 wherein in the filling state of the body the first opening is partially obstructed to an extent which permits airflow therethrough, but which becomes occluded with powder entrained in the airflow.
- 20 4. The capsule of claim 1, 2 or 3 in which the body is a multi-part structure in which parts (3, 5) of the body are moved relative to one another to bring the body to its filling and sealing states.
5. The capsule of claim 4 in which the body is assembled in both the filling
25 and sealing states.
6. The capsule of claim 4 or 5 in which the body has first and second parts (5, 3) which are moved relative to one another to bring the body to its filling and sealing states.
- 30 7. The capsule of claims 5 and 6 wherein in the filling and sealing states the first part is mounted to the second part.

8. The capsule of claim 6 or 7 wherein in the sealing state the first part is disposed in a first position relative to the second part in which it sealingly closes the first and second openings, and wherein in the filling state the first part is
5 disposed in a second position relative to the second part in which it opens the first and second openings.
9. The capsule of any one of claims 6 to 8 when appended to claim 3 in which the first part partially obstructs the first opening in the filling state.
10
10. The capsule of claim 9 in which the first part is partially plugged in the first opening in the filling state.
11. The capsule of claim 10 in which the first part has a plug section (34)
15 which is located in the first opening in the filling state, the plug section having an outer surface (37) which, in the filling state, is at least in part spaced from an inner surface of the first opening.
12. The capsule of claim 11 in which the outer surface has first and second
20 outer surface portions, wherein in the filling state the first outer surface portion (37) is spaced from the inner surface of the first opening and the second outer surface portion abuts the inner surface of the first opening.
13. The capsule of claim 12 in which the first outer surface portion
25 corresponds to one or more channels (37) in the outer surface of the plug section.
14. The capsule of claim 11, 12 or 13 in which the plug section is a first plug
30 section and the first part has a second plug section which sealingly plugs the first opening in the sealing state.

15. The capsule of claim 14 in which the body is moved from the filling state to the sealing state by movement of the first part in a first direction relative to the second part, the first plug section being disposed, in use, on the first part in the first direction relative to the second plug section.
- 5 16. The capsule of claim 14 or 15 in which the first and second plug sections are contiguously arranged.
- 10 17. The capsule of claim 8 or any one of claims 9 to 16 when appended to claim 8 in which the first part sealingly plugs the second opening in the sealing state.
- 15 18. The capsule of any one of claims 6 to 17 in which the first opening is formed in the second part.
19. The capsule of any one of claims 6 to 18 in which the second opening is formed in the second part.
- 20 20. The capsule of claims 18 and 19 in which the second part is a sleeve part with an internal passageway (21) which connects the first and second openings.
21. The capsule of claim 20 in which the first opening is formed by a restriction (25) in the passageway.
- 25 22. The capsule of claim 21 in which the restriction is formed by an inwardly directed shoulder (25) in the passageway.
23. The capsule of any one of claims 20 to 22 in which the second opening is formed at an end of the internal passageway.
- 30 24. The capsule of any one of claims 6 to 23 in which the first part is mounted in the second part for sliding movement relative thereto.

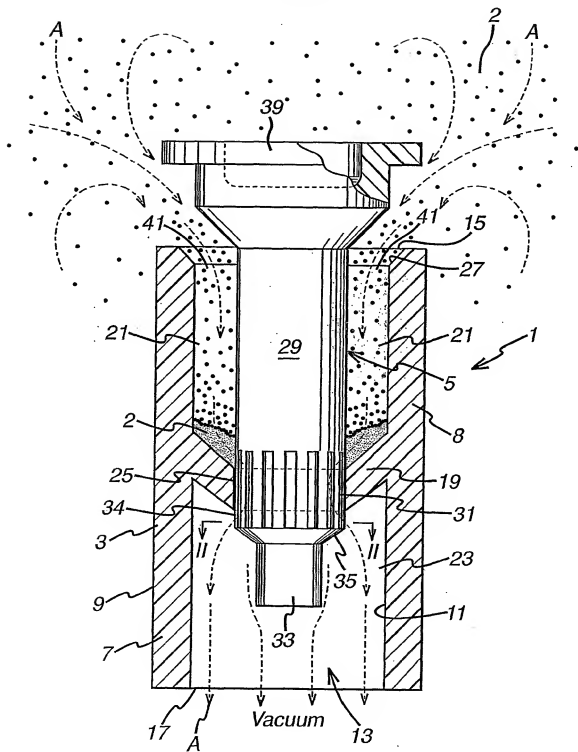
25. The capsule of any one of claims 6 to 24 in which the internal chamber is defined between the first and second parts.
- 5 26. The capsule of any one of claims 20 to 23 in which the first part is slidably mounted in the passageway and the internal chamber is defined between the - inner surface of the passageway and the outer surface of the first part.
- 10 27. The capsule of any one of claims 6 to 26 wherein in the filling state the first part extends through the second opening to leave a gap therebetween for ingress of the entrained powder into the internal chamber and wherein in the sealing state the first part is moved into sealing relation in the second opening.
- 15 28. The capsule of claim 27 in which the first part has a cap section (39) which, in the filling state, is spaced exteriorly of the second opening, but which in the sealing state is sealingly seated in the second opening.
- 20 29. The capsule of claim 28 when appended to claim 11 in which the first part has a shank section (29) connecting the cap section to the plug section.
30. The capsule of any one of claims 6 to 29 in which the first and second parts are further movable relative to one another to bring the body from the sealing state to a discharging state in which an airflow is able to be produced through the body from the first opening to the second opening to entrain the powder in the internal chamber into the exterior environment.
- 25 31. The capsule of claim 30 when appended to claim 11 wherein the first part has a section with a transverse dimension which is less than the corresponding dimension of the plug section, the section being located with respect to the plug section such that in the discharging state it is brought into registration with the first opening.
- 30

32. The capsule of any one of the preceding claims comprising a pharmaceutical powder in the internal chamber.
33. The capsule of claim 32 having a unit dose of the pharmaceutical powder
5 in the internal chamber.
34. The capsule of any one of the preceding claims in which the internal chamber is the sole internal chamber.
- 10 35. An inhalation device comprising one or more capsules according to claim 33 or 34.
36. A method of providing a capsule filled with a powder having the steps of:-
(a) providing a capsule according to any one of the preceding claims in its filling
15 state,
(b) creating an airflow through the body of the capsule in a direction from the second opening to the first opening to cause powder from a powder source disposed externally of the capsule to be entrained into the internal chamber of the body, and
20 (c) moving the capsule to its sealing state.
37. The method of claim 36 in which the powder source is a powder cloud.
38. The method of claim 36 or 37 in which the airflow is created by applying a
25 vacuum at the first opening.
39. The method of claim 36, 37 or 38 in which the powder is a pharmaceutical powder.
- 30 40. The method of any one of claims 36 to 39 applied to a plurality of the capsules simultaneously.

41. The method of any one of claims 36 to 40 applied to a plurality of the capsules so that each capsule contains the same quantity of powder or substantially the same quantity of powder.
- 5 42. A capsule for a powder substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of drawings.
43. A method of filling a capsule with powder substantially as hereinbefore described with reference to, and as illustrated by, the accompanying FIGURES of
10 drawings.

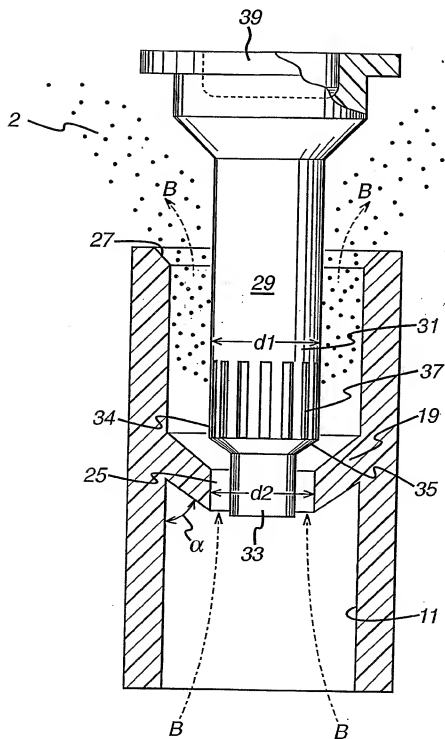
$\frac{1}{3}$

FIG. 1



3/3

FIG. 4



INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/13074

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 1 410 556 A (DORMENT FRANK C) 28 March 1922 (1922-03-28)	1-11, 14-31, 34
A	page 1, line 50 -page 2, line 96; figures 1, 2	36
X	US 2 642 063 A (BROWN FRANK E) 16 June 1953 (1953-06-16)	1
A	column 6, line 11 - line 23; figure 10	36
X	DE 837 157 C (KARL MENDE) 21 April 1952 (1952-04-21)	1
A	page 3, line 85 -page 4, column 4; figure 2	36
A	GB 367 580 A (RONALD HAYDEN LINTON) 25 February 1932 (1932-02-25) the whole document	1, 2, 4-11
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

5 April 2004

Date of mailing of the international search report

22/04/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2220 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Vänttinen, H

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 03/13074

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2 590 832 A (BROWN FRANK E) 25 March 1952 (1952-03-25) the whole document	1
A	US 6 102 036 A (ZAMEL NOE ET AL) 15 August 2000 (2000-08-15) the whole document	1

INTERNATIONAL SEARCH REPORT

international application No.
PCT/EP 03/13074

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 42, 43
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 42,43

Claims 42 and 43 refer only to figures and drawing for defining the subject-matter for which the protection is sought. Such a definition does not allow the determination of the technical features to be searched (Article 6 PCT).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Int onal Application No
PCT/EP 03/13074

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 1410556	A	28-03-1922	NONE	
US 2642063	A	16-06-1953	NONE	
DE 837157	C	21-04-1952	NONE	
GB 367580	A	25-02-1932	NONE	
US 2590832	A	25-03-1952	NONE	
US 6102036	A	15-08-2000	NONE	